MAGNETIC ROD APPARATUS AND METHOD FOR MANIPULATING MAGNETIC PARTICLES FOR DETECTING ANALYTES

CROSS-REFERENCE TO RELATED APPLICATION(S)

[001] This application claims priority to U.S. provisional application No. 60/529,261, entitled METHOD AND APPARATUS FOR DETECTING ANALYTES, filed December 12, 2003.

TECHNICAL FIELD

[002] This disclosure relates to magnetic devices for handling magnetic beads for sample preparation and analysis.

INTRODUCTION

[003] Magnetic particles are widely used in life sciences and biotechnology since they provide substantially increased surface area for interaction with desired analytes and magnetism for easy separation of bound analytes from undesired entities in the solution. These particles are also widely used in medical diagnosis such as immunoassays and nucleic acid based assays.

[004] Several instruments have been developed to accommodate the processes that use magnetic particles. One of them involves the use of an external magnet and a liquid handling system. Separation of magnetic particles and bound analytes is accomplished by placing the magnet near the exterior of a vial or the like, which causes the attachment of magnetic particles onto the vial wall. A liquid handling system then aspirates the liquid solution in the vial. The magnetic particles may be washed with a desired number of times by suspending the particles in fresh solution while the magnet is moved away from the vial, attracting the magnetic particles to the vial wall again, and then aspirating the solution. One variation of this system involves the use of a pipette tip, which removes the entire solution, including the magnetic particles, from the vial followed by moving a magnet near the pipette tip, which results in the attachment of magnetic particles on the pipette tip wall. The liquid solution in the pipette tip is then expelled from the

tip, thereby leaving behind the magnetic particles inside the pipette tip. The pipette tip along with the particles is then moved to another vial containing fresh solution. After moving the magnet away from the pipette tip, the magnetic particles are expelled into the vial through one or more cycles of suctioning and aspiration of the solution in the vial. This step can again be repeated several times to accomplish desired numbers of washes.

[005] The liquid handling system used in these instruments is often expensive to build or installed and is subjected to wearing and tearing, which may incur further expense in maintenance. It is therefore desirable to provide devices and instrument systems that use little or no liquid handling for the identifying analytes attached to magnetic particles.

SUMMARY OF THE DISCLOSURE

[006] Provided herein are magnetic devices for manipulating magnetic particles in a fluid sample that eliminate or reduce the need for fluid transfer operations. One embodiment is an electromagnet disposed within a ferromagnetic tip. The ferromagnetic tip is disposed at an end of a rod and configured to fit within internal dimensions of a fluid sample well. The device includes conductive leads configured for connecting the electromagnet to a current supply. Turning the electromagnet on and off allows for attachment and detachment of magnetic particles containing bound analytes. The electromagnetic rods can be used for transferring the magnetic particles between different sample wells and for washing the magnetic particles within a sample well.

[007] In another embodiment, there is provided a rod comprised of a ferromagnetic material having an upper portion and a lower portion. The lower portion terminates at a tip configured to fit within internal dimensions of a fluid sample well used for processing biological samples in an assay. A conductive coil is formed around the upper portion of the rod to form an electromagnet assembly and has leads for connecting the conductive col to a current source.

[008] In another aspect, there is provided a system that uses the electromagnetic rod devices provided herein for biological assays. The system includes any of the electromagnetic rod devices provided herein in combination with an actuator

assembly configured to move the rod assembly in at least one of a vertical and a horizontal direction. The system is used for automated sample processing and manipulation of magnetic particles in a multi-step assay procedure that transfers magnetic particles from well to well without need to transfer liquid samples.

[009] In yet another aspect, there is provided a method for manipulating magnetic particles in a fluid sample using the devices and systems provided herein. The method includes contacting a fluid sample containing magnetic particles suspended therein, with an electromagnetic rod assembly comprised of a ferromagnetic material dimensioned as a rod having an upper portion and a lower portion, the lower portion terminating in a tip configured to fit within internal dimensions of a fluid sample well. Alternately switching the electromagnet rod assembly on and off alternatively engages and disengages the magnetic particles with at least one of the rod tip, or a tip cover comprised of a non-ferromagnetic material that engages the tip. In one typical embodiment the electromagnet rod engages the magnet particles in a first sample well and disengages the magnetic particles in a second sample well different from the first. The alternate engagement and disengagement may also be performed in a single sample well to facilitate washing of the magnetic particles.

BRIEF DESCRIPTION OF THE DRAWINGS

[010] Figure 1 depicts one embodiment of a magnetic rod device as provided herein.

[011] Figure 2 depicts another embodiment of a magnetic rod device as provided herein.

[012] Figure 3 depicts a magnetic rod device and method of use thereof as provided herein.

[013] Figure 4 depicts a cartridge array of sample wells in a system includes the magnetic rod devices provided herein.

[014] Figure 5 depicts a sample processing system that includes the magnetic rod devices provided herein.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

[015] Provided herein are several embodiments of a magnetic rod device and system for manipulation of magnetic particles suspended in a solution. As used herein, "magnetic particles" means the particles are either magnetic themselves, or are ferro-magnetic and therefore capable of being attracted to a magnet. The devices and systems provided herein are useful for automated or manual washing of the magnetic particles and manual or automated transfer of magnetic particles from one fluid sample well (e.g. vial) to another without using a liquid handling system or magnetic bar externally positioned from the vial. These magnetic rod devices and systems incorporating the same, provide improvements in or to the transfer of magnetic particles during an assay for biological analytes that are bound, or become bound, to the magnetic particles by any of a variety techniques known or later developed in the art. Also provided are methods for detecting analytes in a sample or multiple samples using the magnetic rod devices provided herein.

[016] The magnetic rod device uses an electromagnetic component, which may be embodied in numerous physical shapes including, but not limited to, rod, bar, rectangular, spherical, planar, conical, or cylindrical shapes, or combinations of these shapes. Variations of these physical shapes such as a rod with indentations or the like may be also be included to increase surface area. For the sake of simplicity, the devices provided herein are generally referred to as electromagnetic rods. As used herein, an "electromagnetic rod" is any structure, or combination of structures, having different ends that are separated from one another and where magnetic flux from an electromagnet can be emanated from at least one end. Thus, even a sphere may be configured as an electromagnetic rod within this meaning, if the sphere is either attached to a linear rod, bar or the like, or is configured with an electromagnet in one section of the sphere but not another.

[017] The electromagnetic portion of the electromagnetic rod is normally, but not necessarily, housed or embedded in a chamber or the like, where an electrical lead (e.g., a wire) connects the electromagnet to a power supply. One example embodiment of the electromagnetic rod is illustrated in Figure 1. This

embodiment of the electromagnetic rod 10 includes an electromagnet 12 disposed within a ferromagnetic tip 14. The ferromagnetic tip 14 is disposed at a lower tip portion 13 opposite an upper portion 15 of the electromagnet rod 10. Conductive lead wires 16 for connecting the electromagnet 12 to a current supply source 18 are provided to activate the electromagnet 12. The rod 10 is configured at the lower tip portion 13 to fit within the internal dimensions of a fluid sample well 20.

[018] Optionally, the lower tip portion 13 containing the electromagnet 12 is also configured to removably engage a tip sheath 24 configured to fit within the internal dimensions of a fluid sample well 20. In certain embodiments, the tip sheath 24 is made of a non-ferromagnetic material. The tip sheath 24 permits transmission of magnetic flux from the electromagnet 12 through the tip sheath 24 so that magnetic particles are attracted to, and bind to, the tip sheath 24 without directly contacting the electromagnet rod 10 with fluid in the sample well 20. Thus, the tip sheath 24 protects the electromagnet rod 10 from being contaminated with contaminants from prior uses, allowing repeated use of the same electromagnetic rod 10 for different assays.

[019] Typically, the tip sheath 24 is made of a polymeric plastic material such as polypropylene, polystyrene, polyethylene, polycarbonate and the like. In these embodiments, the tip sheath 24 can removably engage the tip portion 13 of the electromagnetic rod 10 by frictional force alone. In other embodiments, the tip sheath 24, may be configured to engage the tip portion 13 of the electromagnetic rod 10 by corresponding mating elements, such as thread and screw, Luer connections or other easily detachable connector mechanism.

[020] Another example embodiment of an electromagnet rod 110 is illustrated in Figure 2. The lower tip portion 13 of the electromagnet rod 110 terminates in a tip 113 having a cylindrical or spherical cross section. In this embodiment, the cross-sectional perimeter of the tip 113 is greater than the cross sectional perimeter of the upper portion 15, which provides a greater surface area at the tip 113 for collecting magnetic particles. In contrast to the electromagnet rod 10 depicted in Figure 1, the conductive winding 17 (e.g. coil) required for electromagnetic function is not located within the lower tip portion 13 of the

electromagnet rod 110. Rather, the winding 17 is located above the tip 113 in the upper portion 15 of the electromagnet rod 110. This embodiment permits a larger winding 17 around a larger ferromagnetic core 21 within the upper portion 15 so that a stronger magnetic force can be generated. In this embodiment, the entire electromagnet rod 110 acts as the electromagnet but only the lower tip 113 engages the fluid sample well 20. The electromagnetic winding 17 plus core 21 generates magnetism when electrical current pass though the coil, 17 and magnetic flux will emanate from the tip 113. The upper portion 15 of the electromagnetic rod defining the core 21 as well as the tip 113 can be made of any material suitable for this application such as iron or nickel or other ferromagnetic materials.

[021] In certain embodiments, the electromagnetic rod 110, is also configured to fit within the plastic tip sheath 24 that serves as a protective layer for the electromagnetic rod 110 analogous to the electromagnetic rod 10 depicted in Figure 1. In certain embodiment, the tip sheath 24 that sheathes these electromagnetic rods 10, 110 is of a disposable type, which further simplifies magnetic particle transfer process since it makes it possible to eliminate the necessity to wash the electromagnetic rod after completing an assay.

[022] Magnetism of the electromagnetic rods 10, 110 is controlled by a control module 19, which is depicted in Figure 3. The control module 19 minimally contains a switching mechanism that controls a supply of electric current to the windings 17 of the electromagnetic rods 10, 110. Turning on the switch magnetizes the rods 10, 110 while turning off the switch shuts off magnetism. As a result, the supply of electric current causes magnetic particles 9 contained in the sample well 20a to attach to the electromagnet rod 10, 110 or to the tip sheath 24, and consequently permits the transfer of the particles or the like to a different sample well 20b. In addition, repeated turning on or off the switch while the tip portion 13, 113 of the electromagnet rods 10, 110 remains in the same solution causes the magnetic particles 9 to attach and detach from the electromagnet rod 10, 110 causing turbulence in the solution, which facilitates washing of the magnetic particles. The control module 19 may be operated manually, or optionally be configured to be controlled by a separate controller

assembly, or to automatically turn on and off at a user selected interval and/or in response to a movement of the electromagnetic rod 10, 100 to a different sample well 20b.

[023] Another way to wash the magnetic particles 9 is to collect the magnetic particles 9 on the tip portion 13, 113 of the electromagnet rods 10, 110 and move the magnetic rods 10, 110 within the fluid containing sample well 20. An advantage of this approach is that the magnetic particles are attached over a broad surface area at the end of the electromagnetic rod 10, 110 allowing efficient washing of the magnetic particles 9. In optional embodiments, the electromagnet rod 10, 110 may be attached to an actuator module 30 that moves the electromagnet rod up and down in a vertical direction, side to side in horizontal direction, rotationally about a longitudinal axis, or any combination of the same. In typical embodiments, movement in the vertical direction is independently controlled from movement in the horizontal direction. Thus, for example, a vertical movement may be used to wash the magnetic particles 9 attached to the electromagnet rod 10, 110 in one sample well 20a, while a horizontal movement may be used to transfer the electromagnet rod 10, 110 to a different sample well 20b. Of course, any combination of movements of the electromagnetic rod 10, 110 can be used in various embodiments to accomplish different purposes.

[024] In certain embodiments, the electromagnetic rod 10, 110 with or without the tip sheath 24 is used in an assay system, where all necessary reagents are pre-filled into a cartridge 26 that includes an array of sample wells 20_1-20_{14}, that include desired reagents in a desired quantity or volume as depicted in Figure 4. Preferably the cartridge 26 is in the shape of a strip or a row consisting of multiple wells 20_1-20_{14}, which are typically, but not necessarily, molded as a single unit. Thus, a single cartridge 26 is sufficient for carrying multiple steps as may be required for various protocols for detecting analytes in a sample. In certain embodiments, the disposable sheath 24 for the electromagnetic rod 10, 110 is initially provided in one of the sample wells 20a in the cartridge 26 as depicted in Figure 4. The individual sample wells 20_1-20_{14} in the cartridge 26, or the whole cartridge 26 may optionally be sealed with a film 32, which is

substantially air/water-impermeable and resistant to a certain pressure without breaking. The film 32 on the cartridge 26 can be punctured with the tip 13, 113 of the electromagnetic rod 10, 110, by the disposable tip sheath 24 or, in other embodiments, with a separate puncturing point 28 or cutting blades, which can be attached to the same linkage that connects the electromagnetic rod 10, 110 to an actuating device 30 on a suitable instrument system. It is understood that this puncturing point 28 can be a durable one or a disposable one, and can optionally be configured to pick up the piece of film 32 detached from the cartridge 26 after puncturing.

[025] The disposable tip sheath 24 may be housed in any position in the cartridge 26, but preferably in the first well 20a since the electromagnetic rod 10, 110 engages the tip sheath 24 before proceeding to the next operational step. If no disposable tip sheath 24 is used, the tip portion 13 of the electromagnet rod 10, 110 can optionally be coated with Teflon or the like, and a washing can be performed between tests. The washing solvent can also be pre-filled into the cartridge 26. One or more fluid sample wells 20_1-20_{14} in the cartridge 26 are normally pre-filled with reagents for sample processing, e.g., for sample lysis and binding of analytes to magnetic particles, other analyte binding reagents and/or detection reagents, washing reagents and the like, as may be required for analyte capturing on the magnetic particles in a variety of different protocols. In certain situations, however, it may be preferable to have a separate vial for certain steps in the sample processing, which may permit, for example, combining multiple samples into a single vial for higher sample loading volume.

[026] As well known to a skilled person in the art, the magnetic particles 9 can be coated with a variety of analyte binding ligands such as antibodies, antigens or nucleic acids that form one partner in a binding pair that ultimately associates the bound analyte with a detectable marker. Specific analyte binding ligands enable the detection of particular analytes by specific binding to the analyte. Other types of non-specific interactions such as ion paring, hydrophilic absorption, hydrophobic interaction, hydrogen binding and etc, can also be incorporated to the surface of the magnetic particles and used for selective, although non-specific binding of desirable analytes.

[027] In another aspect, there is provided, an instrument system 50 that performs the entire analyte detection process including magnetic particle transferring, incubation at various conditions if necessary, and detection, as depicted in Figure 5. Preferably, the instrument system 50 is controlled with an on-board microprocessor or off-board computer 40 or some combination of electro-mechanical control elements. The system also may include a detector 52 may be placed near or underneath any desired well or wells 20_1-20_{14} in the cartridge 26. There may be only one detector 52 in the instrument system 50, in which case, the detector 52 or the cartridge 26 can move relative to one another to complete detection in multiple cartridges 26 in an automated system. However, more than one detector 52 can also be used to accommodate higher sample throughput. The instrument system 50 may further include a heating system to provide desired temperature, either isothermal or variable, to the wells of the cartridge 26. As mentioned above, the cartridge 26 typically contains one or more wells 20_1-20_{14} pre-filled with reagents for processing separate samples. In certain situations, however, a separate vial for sample processing may be used, in which case the instrument system 50 would have a sample vial holder that permits multiple samples to be combined in a single sample vial, for example, for sample lysis or analyte capturing.

[028] In various embodiments, the electromagnetic rod 10, 110 can be instructed by movement controller to perform movement, via actuator assembly 30, for example, a vertical movement, once or repeatedly in the well 20 with magnetic particles 9 attached to the tip 13, 113 or sheath 24, (on-mode: with magnetism) or with magnetic particles in the solution (off-mode: no magnetism). Such movements serve to improve particle washing or particles mixing in the solution.

[029] In yet other embodiments, the electromagnetic rod 10, 110 may be configured with a second electrical lead 60 for connection to one pole of a power supply to impart electrical polarity to the electromagnetic rod 10, 110. In this case the electromagnetic rod 10, 110 also serves as an electrode than can either be positively or negatively charged (or alternating between the two). Another electrode 62 charged with the opposite polarity may also be provided in, or near, a sample well 20 in the cartridge 26 to create an electric field, which may be

switched on or off. When the electric field is on, and with desired polarity, undesirable entities may be made to migrate away from the magnetic particles 9 that are attached to the tip 13, 113 of the electromagnetic rod 10, 110, whereas the entities can be made to migrate toward the tip 13, 113. The analytes attached to the ligand on the magnetic particles 9 attached to the tip 13, 113 remain bound to the magnetic particles 9 through their specific interaction. For example, when the electromagnetic rod 10, 110 is positively charged, negatively charged DNA will migrate towards it, and therefore speed up the capture of the DNA by magnetic particles 9 attached to the magnetic rod 10, 110. Conversely, when the electromagnetic rod 10. 110 is negatively charged, it will repel non-specifically bound DNA thereby reducing non-specific binding of undesirable DNA. Similarly, charged proteins or other charged analytes may also be subjected to this process.

[030] In a still further embodiment, a second electromagnetic source 64 that can be switched on and off can also be installed under or near the cartridge 26 in the instrument system 50. By working in coordination with the electromagnetic rod 10, 110, magnetic particles 9 can be induced to migrate back and forth between the two sources of magnetism, which may improve washing efficiency.

[031] It is understood that the detector 52 installed in the instrument system 50 can be any detector suitable for the analyte detection methodology used. Typical detectors include, but are not limited to, a luminometer, fluorescence detector, electro-chemiluminescent detector, radioactivity detector, or colorimetric detector. It is also understood that more than one unit of detectors 52 can be installed in the instrument system 50. It is further understood that the instrument system 50 may not have a detector, in which case detection of analytes is performed with a stand-alone detector and the instrument system essentially functions as a separation/purification device. For example, the instrument system can be used to bind and purify target nucleic acids to magnetic particles. The captured target nucleic acids can then be subsequently amplified using the polymerase chain reaction (PCR) or other suitable technique prior to analysis or detection. The instrument system 50 using the electromagnetic rods 10, 110, and cartridges 26, provided herein may be used in a sequential protocol with

different purposes, for example, first to obtain and purify the target nucleic acid, then to amplify the target and then finally to detect the target, because it is known that each of these steps can be made to depend on the use of magnetic particles that need to be treated to different steps in a protocol.

Example 1

Reagent compositions for an analytical cartridge

[032] Provided in Table 1 is an example of the reagent composition for a cartridge. In this example, the cartridge has 13 wells. It is understood of course, that the number of wells in the cartridge can be reduced or increased or that the wells in cartridge can be provided in a micro titer plate, or in a variety of shapes and sizes. Thus, the current example is merely illustrative of one example composition.

[033] Well 1 houses a plastic tip or the like that provides the protective tip sheath for the electromagnetic rod. Although this protective sheath can be placed in any location of the cartridge, it is typical to provide in the first well.

[034] Well 2 contains the lysis buffer and buffering components that will promote binding of nucleic acid type of analytes to complementary capturing sequences. Preferably, the lysis buffer is a medium where nucleic acid hybridization can efficiently occur so that the analyte can be efficiently captured onto the magnetic particles that are coated with the capturing nucleic acids. When used for immunoassays, Well 2 is pre-filled with dilution or conditioning buffer, which is efficient in promoting specific binding of analytes (antigens or antibodies) to magnetic particles coated with specific antigens or antibodies.

[035] Well 3 is contains a suspension with the desired amounts of magnetic particles with containing specific capturing nucleic acid sequences attached thereto for analyte capturing.

[036] Wells 4-6 contain wash buffers for washing magnetic particles attached to captured analytes. The wash buffers may or may not be the same in all wells.

[037] Well 7 is pre-filled with desired amounts of a detection binding reagent or reagents. These reagents normally contain one or more molecules such as antibodies or antigens that can specifically bind to captured analytes. These molecules are normally labeled with a detectable marker such as fluorescent

compounds, chemiluminescent compounds, radioisotopes, or enzymes that can generate or convert a substrate into a detectable signal. It is understood that the markers may or may not be directly conjugated to the detection reagents (antibodies or antigens). An example detection reagent is microparticle coated both with the detectable marker and with specific detection reagents. The detectable markers may being coated on the surface of microparticles or encapsulated within the particles.

[038] Wells 8-11 are pre-filled with wash buffers for washing the complex formed between the magnetic particles, the analyte and the detection reagents. These wash buffers may or may not be the same in each well.

[039] Wells 12 and 13 are pre-filled with detection development solutions. For example, if the detection system relies on coupling to a chemiluminescent assay, the detection development solution would include the appropriate enzymes and substrates for the chemiluminescent reaction. It is understood that none, one or more of these detection development solutions may be needed depending on the markers and detection methods used.

Table 1

Kit Components and Key Ingredients

	Well No.	**Reagent**	Function
Test Cartridge	**1**	Plastic sheath	For providing a protection sheath to the electromagnetic rod
	2	Lysis/Binding Buffer	For lysis, dilution and/or conditioning of samples to be tested.
	3	Magnetic Particles	For capturing of desired analyte(s).
	4-6	Wash buffer(s)	For washing away undesired entities.
	7	Detector reagent	For detection of analytes captured onto magnetic particles.
	8-11	Wash buffer(s)	For washing away undesired entities.
	12	Detection Solution A	Provided if needed for marker detection.

	13	Detection Solution B	Provided if needed for marker detection

Example 2

Protocol and system for the detection of HIV ribonucleic acid

[040] This exemplary protocol is for detecting HIV-1 (human immunodeficiency type 1 virus) ribonucleic acid (RNA), which is indicative of viral infection. The quantitative level of HIV-1 RNA in a patient's sample, which is normally plasma or serum, can be indicative of therapeutic efficacy if the patient is taking anti-HIV drugs.

[041] Magnetic particles are coated with one or more oligonucleotide types, normally 20-30 bases long, which are complementary with respective regions of HIV-1 genome. It is understood that these oligonuclotides can be extended with non-complementary bases, normally deoxythymidine (dT), to improve binding efficiency with HIV-1 genome.

[042] The detection reagents used here are also one or more oligonucleotide types, normally 20-30 bases long, that are complementary with respective regions of HIV-1 genome but that are distinct from those on magnetic particles. These oligonucleotides may be extended with deoxythymidine as well. These oligonucleotides are covalently coupled to polystyrene particles of desired size. The marker used in this exemplary protocol is acridinium, which is a chemoluminescence chemical. Acridinium is either encapsulated in, or coated onto the surface of, the same polystyrene particles that are coated with HIV-1 specific oligonucleotides.

[043] It is understood that this exemplary protocol can be further modified as required. The detection procedure is as follows:

1. Puncture a small hole in the second well (well 2), which contains the lysis/binding buffer. Load the desired amounts of samples to the well and place the cartridge into the cartridge holder.
2. The following procedure is completed automatically with the instrument:
   a. Puncture holes on the wells in the entire cartridge.

b. Heat the sample well for 5 minutes at 80-90°C to lyse any cells, inactivate Rnase, and denature the secondary structure of HIV-1 RNA.

c. Cool the temperature to 50°C for 5 minutes.

d. Clothe the electromagnetic rod with the plastic sheath in well 1 by inserting the rod into the sheath.

e. Use the electromagnetic rod to pick up magnetic particles in well 3 by inserting it into the well 3 with electrical current on, transfer the particles to well 2 by withdrawing the rod from well 3 and re inserting it into well 2, release the particles by switching off electromagnetism, and move the electromagnetic rod up and down the well three times to mix the particles.

f. Incubate at 50°C for 15 minutes with intermitting mixing (e.g., once every 3 minutes) or at desired temperature and for desired duration.

g. Switch on electromagnetism, pick up the magnetic particles in well 2, and transfer to well 4, which contains wash buffer.

h. Magnetic particles are released and recaptured onto the electromagnetic rod. Alternatively, magnetic particles are not released to the solution but rinsed in the solution by moving the electromagnetic rod up or down the solution.

i. Repeat the wash procedure in wells 5 and 6.

j. Transfer the magnetic particles to well 7, mix and incubate at 50°C for 15-20 minutes, or at desired temperature and incubation duration.

k. Repeat the wash step using solutions in wells 8-11.

l. Release the particles to well 12, which contains hydrogen peroxide at lower pH (e.g., 5 mM HCl). If there is any detectable HIV-1 RNA in the sample, certain numbers of polystyrene particles marked with acridinium will be carried to well 12.

m. To detect the presence of acridinium, a sufficient amount of sodium hydroxide is injected to well 12, which triggers the

chemoluminescence reaction. The released light is detected with the luminometer component. The presence of HIV-1 (positivity) is determined by comparing the light signal from the sample to one or more negative control.

[044] The disclosure provided herein is illustrative only, and does not limit the scope of uses or embodiments of the inventive devices, systems and methods that have been disclosed. One of ordinary skill in the art can make numerous modifications or additions and can embody the invention in a wide variety of forms.